P16671.A07

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : A. ITAI et al.

Serial No : Not Yet Assigned

Filed : Concurrently Herewith

For : DESIGN METHOD OF PHYSIOLOGICALLY ACTIVE COMPOUND

PRELIMINARY AMENDMENT

Commissioner of Patents and Trademarks
Washington, D.C. 20231

Sir:

Prior to the examination of the above-identified patent application, the Examiner is respectfully requested to amend the claims as follows:

IN THE SPECIFICATION

Please amend the specification as follows:

Page 1, before line 1 and immediately following the title, insert the following:

---CROSS-REFERENCE TO RELATED APPLICATION

This application is a continuation of Application No.09/068,459, filed May 12, 1998, which is the National Stage of International Application No. PCT/JP96/03325 filed November 13, 1996, published in the Japanese language, and claims priority of Japanese Application No. 7-294189 filed November 13, 1995. The entire disclosure of Application No. 09/068,459 is considered as being part of the disclosure of the disclosure of this application, and the entire disclosure of Application No. 09/068,459 is expressly incorporated by reference herein in its entirety.---

IN THE CLAIMS

Please amend claims 5, 6 and 8 as follows (*Marked-Up Copies of the Claims are Herein Attached as Amended*):

5. The method of claim 3 which comprises a step (b) of constructing structures of the query cmpounds by an automatic structure construction method.

6. The method of claim 3 wherein the step (a) comprises either or both of the following two steps:

(c) a step of first screening by selection of trial compounds based on one or more parameters selected from a group of parameters consisting at leasty of number of atoms, number of bonds, number of ring structures, number of atoms for each atomic type and molecular weight; and/or

(d) a step of second screening by matching of candidate compounds selected in the first screening step for mode of covalent bonds.

8. The method of claim 3 wherein, after the step (a), a third screening is performed by the following step (f):

(f) a stepof selecting one or more preferred lead-candidate compounds by estimating binding schemes to the biopolymer for the lead-candidate compounds selected in the step (a) based on three-dimensional information and binding schemes of the query molecules to the biopolymer, and calculating one or more parameters relating to interaction between the lead-candidate compounds and the biopolymer; and/or the following step (g):

(g) a step of selecting one or more preferred lead-candidate compounds by supposing a virtual

receptor model which represents physiochemical environment of the ligand binding site of the biopolymer based on information of three-dimensional structures of one or more known ligands capable of binding to the biopolymer, and then judging goodness of fit to the virtual receptor model for the lead-candidate compounds selected in step (a).

Respectfully submitted,
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MARKED-UP COPY OF THE CLAIMS

5. The method of claim 3 [or 4] which comprises a step (b) of constructing structures of the query cmpounds by an automatic structure construction method.

6. The method of [any of claims 3 to 5] claim 3 wherein the step (a) comprises either or both of the following two steps:

(c) a step of first screening by selection of trial compounds based on one or more parameters selected from a group of parameters consisting at leasty of number of atoms, number of bonds, number of ring structures, number of atoms for each atomic type and molecular weight; and/or

(d) a step of second screening by matching of candidate compounds selected in the first screening step for mode of covalent bonds.

8. The method of [any of claims 3 to 7] claim 3 wherein, after the step (a), a third screening is preformed by the following step (f):

(f) a stepof selecting one or more preferred lead-candidate compounds by estimating binding schemes to the biopolymer for the lead-candidate compounds selected in the step (a) based on three-dimensional information and binding schemes of the query molecules to the biopolymer, and calculating one or more parameters relating to interaction between the lead-candidate compounds and the biopolymer; and/or the following step (g):

(g) a step of selecting one or more preferred lead-candidate compounds by supposing a virtual receptor model which represents physiochemical environment of the ligand binding site of the biopolymer based on information of three-dimensional structures of one or more known ligands capable of binding to the biopolymer, and then judging goodness of fit to the virtual receptor

model for the lead-candidate compounds selected in step (a).